function was observed with increasing doses from 250 to > 1250 mg/kg/day. Doses of 250 to 750 mg/kg/day resulted in mild to marked impairment of ADP induced AGG, markedly decreased ADS, and moderately prolonged PF 3 clotting times. Collagen induced AGG was impaired and the BT was prolonged only at doses > 750 mg/kg/day. Platelet dysfunction was evident at 4 hr., significant at 24 hr., and maximal at 72 to 96 hr. with little further progression up to 14 days despite continued treatment. At equivalent doses CARB was slightly more inhibitory than TIC. EM, 5HT, and AN did not change significantly. Platelet function was significantly improved 24 hr. after treatment was discontinued, and progressive improvement continued for 5 to 14 days.

These studies demonstrate that CARB and TIC induce a dose-related impairment of platelet function. They suggest that these drugs interfere with the platelet release reaction. They indicate that CARB and TIC are promising anti-thrombotic agents which merit further study.

L. L. Houbouyan, J. F. Stoltz and A. F. Goguel (Hôpital A. Paré, F 92100 Boulogne, France):
Antibiotics, Platelet Aggregation and Electrophoretic Mobility. **(86)**

The *in vitro* influence of twelve antibiotics (representing the principal classes: β-lactam group, aminoglycosides, polypeptidic antibiotics, antimitotics, . . .) on the ADP-induced Platelet Aggregation, the Screen Filtration Pressure test and the liquid phase Electrophoretic Mobility (E. M.) has been studied. According to the results formerly obtained on the interference Penicillin G-platelets, the authors have mainly investigated the β-lactam group (Penicillin G, Ampicillin, Carbenicillin, Cefalotin, Metampicillin, Methicillin, Oxacillin, . . .). This group seems particularly interesting as an antiaggregating effect has been found out for most of them; a parallel decrease of the E. M. has been generally observed.

In attempts to elucidate the mechanism of physiochemical interaction with the membrane, the competitive effect of phospholipases and Penicillin G has been studied. The results seem to point out an interference of this antibiotic with the membrane phospholipids; this could be in accordance with the rheological data of Padefield and Kellaway. The interference with some other membrane groups has also been considered (carboxyl, phosphates . . .).

An *in vivo* study has also been realized on patients massively perfused with some of these antibiotics (especially Penicillin G, Carbenicillin . . .).

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J. C. Ferrand, D. Aubert, B. Lacaze, O. Pepin, J. J. Thebault (*Parcor*, Département Recherche et Développement, F 31023 Toulouse Cedex, Centre Hospitalier Intercommunal de Créteil): **In Vivo Activity of Tieclopidine, a New Drug with Platelet Aggregation Inhibiting, Antisludge and Antithrombotic Properties.** **(87)**

Tieclopidine (53–32 C) belongs to a new series of synthetic compounds which have proved to inhibit significantly blood platelet aggregation in animals. Administered orally to rats, it reduces markedly the plate let aggregation induced by ADP and collagen. The activity appears 2 to 6 hours after a single dose and persists for 24 hours.

The sludge and blood stasis induced in rats by protamin sulfate injections disappear completely in five minutes after an intravenous administration of Thieclopidine. Animals pretreated orally with this compound failed to show any sludge formation.

The antithrombotic activity of Tieclopidine was demonstrated in rats carrying a dental broach implanted in the abdominal aorta. White thrombideveloped locally in the control animals, but were absent or much less severe in pretreated animals.

In man the first clinical approach has shown that at a daily dose of 1 g the inhibitory effect of Tieclopidine on ADP induced aggregation requires 24 to 48 hrs to become significant and reaches a plateau after 5 or 6 days of treatment.